

SELENIUM STABILIZED CARBENIUM IONS.
 LEWIS ACID MEDIATED SELENO-ALKYLATION OF KETONES.

K.M. Nsunda and L. Hevesi*

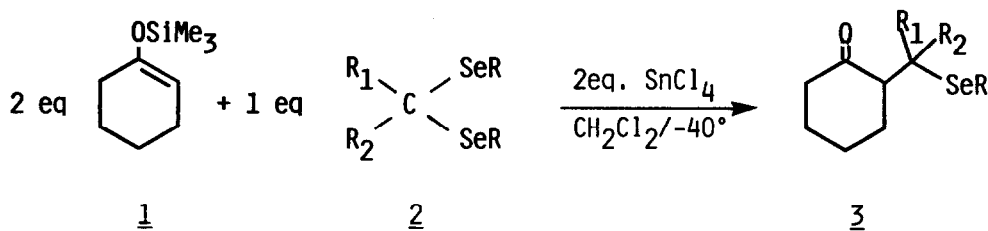
Department of Chemistry
 Facultés Universitaires Notre-Dame de la Paix
 61, rue de Bruxelles, B-5000 NAMUR, Belgium

Silyl enol ethers of ketones can be successfully selenoalkylated by Lewis acid activated seleno-ketals; the product β -seleno-ketones undergo interesting oxidation-deselenation reactions.

We have shown recently that carbenium ions are efficiently stabilized by two methylseleno groups ¹ and that 1,3-bis(seleno)-propenes ² as well as 1-bromo-2-phenylseleno-2-propenes ³ can be activated by a suitable Lewis acid for the introduction of selenium stabilized allyl cation equivalents into electron rich aromatic rings such as furan, ^{2,3} pyrrole, ^{2,3} thiophene ³ and trimethoxybenzene. ³

In this letter we wish to report our preliminary results on the in situ production of saturated carbenium ion like intermediates stabilized by a single selenium atom which carry out seleno-alkylation of silyl enol ethers in good to excellent yield (Scheme I). ⁴

Scheme I



	R	R ₁	R ₂	React. Time(Hr)	Yield (%) in <u>3</u> (*)
<u>a</u>	Me	Me	Me	1.5	84
<u>b</u>	Me	Ph	H	2	89
<u>c</u>	Me	Ph	Me	4	81
<u>d</u>	Me	Et	Me	1.5	61
<u>e</u>	Me	Et	Et	1.5	49
<u>f</u>	Ph	Me	Me	1.5	97

(*) Isolated Yields, calculated with respect to 2

In a typical experiment 0.24 ml (2×10^{-3} moles) of SnCl_4 are dissolved in 1.5 ml CH_2Cl_2 under argon and cooled to -40°C . Addition of a solution of 230 mg (10^{-3} mole) of 2,2-bis(methylseleno)-propane in 0.5 ml CH_2Cl_2 is followed by 340 mg (2×10^{-3} moles) of 1-trimethylsilyloxycyclohexene dissolved in 0.5 ml of the same solvent. After 1.5 hrs of stirring at -40°C , the reaction is quenched with aqueous bicarbonate. Extraction with ether and purification (SiO_2 plate, eluent ether/pentane 10/90) yields 195 mg of ketone 3a as a pale yellow liquid (84 %).

If only 1 eq. of silyl enol ether is reacted with 1 eq. of selenoacetal, the reaction times are significantly longer (6-10 hrs) and the yields are somewhat lower (ca. 70 % for 3a) and some diselenide can be isolated from the product mixture.

Scheme I shows that encumbering of the cationic center with bulkier R_1 and R_2 groups inhibits the reaction (entries d and e), while the presence of a phenyl group makes the formation of the cation easier and 3b and 3c are obtained in high yield. Also, the presumed less effective stabilization of the carbenium ion by a phenylseleno group (entry f) without causing steric inhibition, seems to make of such precursor seleno-acetal excellent alkylating agents.

Among the few other Lewis acids we have tried tin tetrachloride appeared to be the best suited for our purposes. Thus TiCl_4 at -40°C gives only 17 % of 3a after 2.5 hrs of reaction, decent yields could however be arrived at 0°C (71 % of 3a together with some dimethyl diselenide). Use of mixtures of TiCl_4 and $\text{Ti}(\text{OiPr})_4$ as well as of silver salts gave rise to sluggish reaction mixtures from which variable amounts of products 3, starting acetals 2 and diselenides could be isolated. Further characteristics of these alkylation reactions are illustrated in Scheme II.

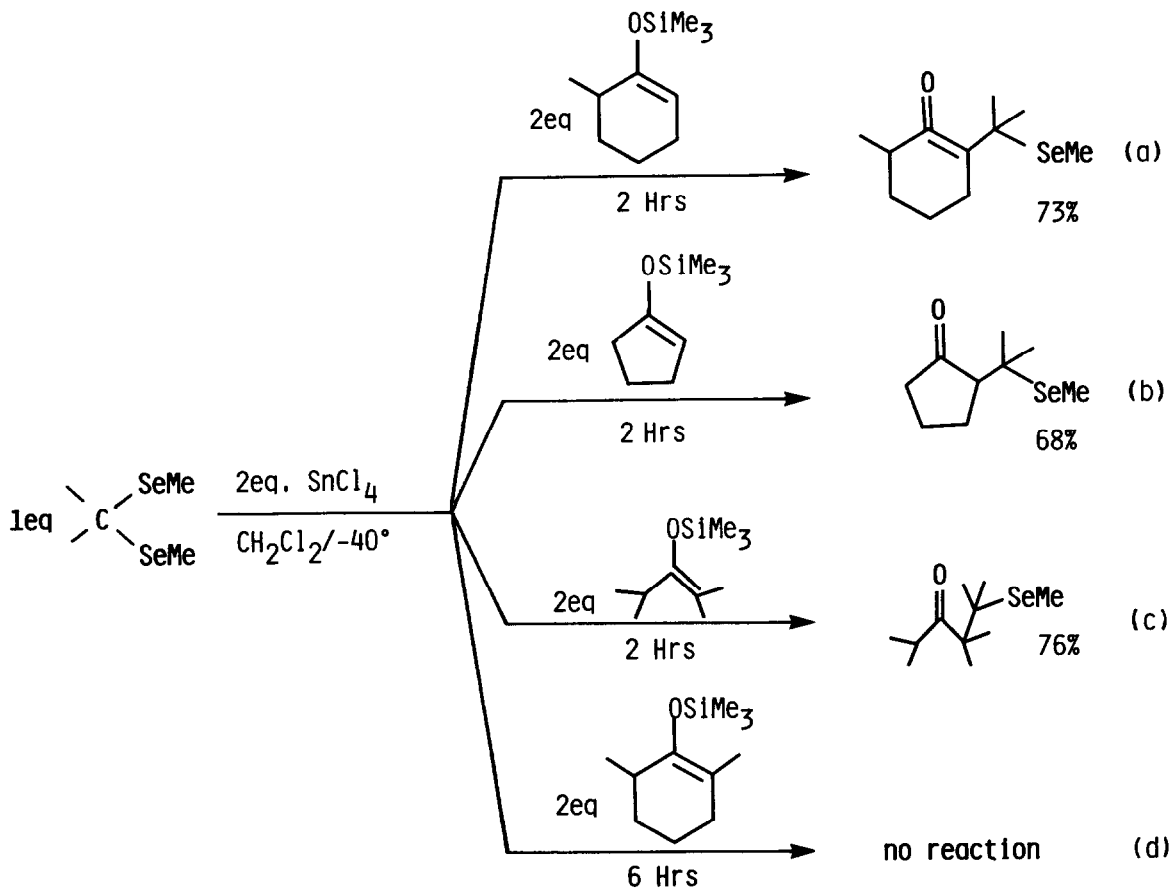
Seleno-alkylation of 1-trimethylsilyloxy-6-methyl cyclohexene proceeds in good yield and totally regioselectively (Scheme IIa) ; it is also efficiently applied in the case of 1-trimethylsilyloxycyclopentene (Scheme IIb).

While steric crowding of the silyl enol ether does not seem to inhibit the alkylation reaction significantly in the case of open chain compounds (Scheme IIc), we were unable to detect the expected product in the case of 1-trimethylsilyloxy-2,6-dimethyl cyclohexene (Scheme IIId) even after prolonged reaction times.

A further limitation of these seleno-alkylation reactions has been encountered in the case of the selenoacetals 2 derived from aldehydes ($\text{R}_1 = \text{alkyl}$, $\text{R}_2 = \text{H}$ or $\text{R}_1 = \text{R}_2 = \text{H}$). Indeed, neither 1,1-bis(methylseleno)-ethane nor bis(methylseleno)-methane did produce 3 when reacted with 1 under the usual conditions. This surprisingly strong effect of the R_1 and R_2 substituents needs further investigation.

In spite of the large amount of work that has already been devoted to and the most valuable results reported for Lewis acid mediated alkoxyalkylation⁵ and thioalkylation⁶ of carbonyl compounds, we believe that our selenoalkylation reactions are interesting in several respects. They represent a new route to β -seleno carbonyl compounds, which were only accessible until now through Michael addition of selenols to α,β -unsaturated carbonyl

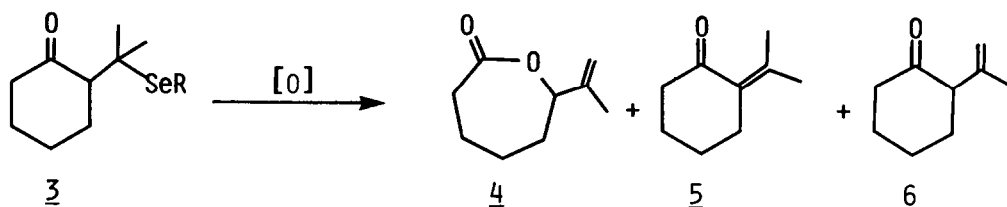
Scheme II



derivatives. Compounds of type 3 may in principle be further transformed in many different ways ; one of these is illustrated in Scheme III. The well known selenoxide elimination leads to 5, while to our knowledge, formation of 4 is an unprecedented reaction.⁷

Work is in progress to extend the scope of the selenoalkylation reactions and to investigate subsequent transformations of the product β -selenocarbonyl compounds.

Scheme III



R	Conditions (oxydant/ t° / time)	4 (%)	5 (%)	6 (%)
Ph	10eq. $\text{H}_2\text{O}_2/\text{THF}/0^\circ/10$ min	62	trace	trace
Me	10eq. $\text{H}_2\text{O}_2/\text{THF}/0^\circ/10$ min	58	14	4
Me	10eq. $\text{H}_2\text{O}_2/\text{THF}/-78^\circ/15$ min	45	23	10
Me	10eq. $\text{H}_2\text{O}_2/\text{THF}/-100^\circ/15$ min	trace	69	trace
Me	1.2eq. mCPBA/ $\text{CH}_2\text{Cl}_2/-78^\circ/15$ min	0	72	trace
Me	4eq. tBuOOH/8eq. $\text{Al}_2\text{O}_3/\text{THF}/-78^\circ/2$ hrs	0	80	0

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References and notes

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- More details will be reported in a forthcoming full paper.

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